

METHOD AND SYSTEM FOR MAMMALIAN JOINT RESURFACING

5

CROSS REFERENCE TO RELATED APPLICATIONS

The present application is a continuation of an international patent application filed 28 August 2001 and assigned Serial No. PCT/US01/41908 which application has not yet been published and which itself is a continuation-in-part of Provisional US Application Serial No. 60/228,444, filed August 28, 2000, the entire disclosures of which are incorporated herein by reference.

10

TECHNICAL FIELD

In one aspect, this invention relates to biomaterials formed *ex vivo* for implantation and use within the body. In another aspect, the invention relates to *in situ* curable biomaterials. In yet another aspect, this invention further relates to the field of orthopedic implants and prostheses, and more particularly, for implantable materials for use in orthopedic joints.

BACKGROUND OF THE INVENTION

20

Applicant has previously described, *inter alia*, prosthetic implants formed of biomaterials that can be delivered and finally cured *in situ*, e.g., using minimally invasive techniques. See for instance, U.S. Patent Nos. 5,556,429, 5,795,353, 5,888,220, 6,079,868, 6,140,452, 6,224,630 and 6,248,131 as well as published International Application Nos. WO 95/30388 and WO 97/26847 and International Application PCT/US97/20874 filed 11/14/97 (the disclosures of each

of which are incorporated herein by reference). Certain of these applications describe, *inter alia*, the formation of a prosthetic nucleus within an intervertebral disc by a method that includes, for instance, the steps of inserting a collapsed mold apparatus (which in a preferred embodiment is described as a "balloon") through a cannula that is itself positioned through an opening within the annulus, and filling the balloon with a flowable biomaterial that is adapted to finally cure *in situ* and provide a permanent disc replacement. See also, Applicant's "Porous Biomaterial and Biopolymer Resurfacing System" (PCT/US99/10004), as well as "Implantable Tissue Repair Device (PCT/US99/11740), and "Static Mixer" (PCT/US99/04407) applications.

See also, US Patent Nos. 3,030,951 (Mandarino), 4,203,444 (Bonnell et al.), 4,456,745 (Rajan), 4,463,141 (Robinson), 4,476,293 (Robinson), 4,477,604 (Oechsle, III), 4,647,643 (Zdrahala), 4,651,736 (Sanders), 4,722,948 (Sanderson), 4,743,632 (Marinovic et al.), 4,772,287 (Ray et al.), 4,808,691 (König et al.), 4,880,610 (Constanz), 4,873,308 (Coury et al.), 4,969,888 (Scholten et al.), 5,007,940 (Berg), 5,067,964 (Richmond et al.), 5,082,803 (Sumita), 5,108,404 (Scholten et al.), 5,109,077 (Wick), 5,143,942 (Brown), 5,166,115 (Brown), 5,254,662 (Szycher et al.), 5,278,201 (Dunn et al.), 5,525,418 (Hashimoto et al.), 5,624,463 (Stone et al.), 6,206,927 (Fell), and EP 0 353 936 (Cedar Surgical), EP 0 505 634 A1 (Kyocera Corporation), EP 0 521 573 (Industrial Res.), and FR 2 639 823 (Garcia), WO 93/11723 (Regen Corporation), WO 9531946 (Milner), WO 9531948 (Kuslich).

Applicant's PCT Application No. PCT/US97/00457 (WO 9726847A1) includes the optional use of a mold, such as a balloon, and describes the manner in which "[t]he mold created within the joint is preferably of sufficient shape and dimensions to allow the resulting cured biomaterial to replace or mimic the structure and function of the removed fibrocartilage. The mold can be formed of synthetic and/or natural materials, including those that are provided

exogenously and those provided by the remaining natural tissues. The mold can either be removed from the site, upon curing of the biomaterial, or is sufficiently biocompatible to allow it to remain in position.”

Applicant’s later PCT Application No. PCT/US97/20874 (WO 9820939A2) further
5 describes the manner in which “ ‘mold’ will refer to the portion or portions of an apparatus of the invention used to receive, constrain, shape and/or retain a flowable biomaterial in the course of delivering and curing the biomaterial *in situ*. A mold may include or rely upon natural tissues (such as the annular shell of an intervertebral disc) for at least a portion of its structure, conformation or function. The mold, in turn, is responsible, at least in part, for determining the position and final dimensions of the cured prosthetic implant. As such, its dimensions and other physical characteristics can be predetermined to provide an optimal combination of such properties as the ability to be delivered to a site using minimally invasive means, filled with biomaterial, and optionally, then remain in place as or at the interface between cured biomaterial and natural tissue. In a particularly preferred embodiment the mold material can itself become integral to the body of the cured biomaterial.”

Applicant’s own use of such mold apparatuses to date has concentrated largely on the use of thin, extensible balloons adapted to be positioned and then filled *in situ* with curable biomaterial, with particular use as a replacement for the intervertebral disc following microdiscectomy. In turn, there has been considerably less focus, to date, on the use of any such
20 molds in other joints, such as the knee. Figures 6 and 7 of Applicant’s PCT Publication No. WO 920939 A2, for instance, shows a balloon and corresponding drilling template for use in knee surgery, the balloon having foot portions protruding from a generally ovoid inflatable portion.

20090901-03502
20090901-03502

Finally, US Patent No. 6,206,927 describes a self-centering meniscal prosthesis device suitable for minimally invasive, surgical implantation into the cavity between a femoral condyle and the corresponding tibial plateau is composed of a hard, high modulus material shaped such that the contour of the device and the natural articulation of the knee exerts a restoring force on the free-floating device. In what appears to be a related manner, Sulzer has introduced a unicompartmental interpositional spacer to treat osteoarthritis in the knee. See “Little Device Could Pack a Big Punch”, Sulzer Medica Journal Edition 2/2000 (www.sulzermedica.com/media/smj-full-tex/2000/0002-full-text-6.html). The device is described as a metallic kidney-shaped insert which fills in for the damaged cartilage between the femur and the tibia.

Such a metallic device, as described in either the Fell patent and/or Sulzer’s product literature, is described as appropriate for use in younger patients with moderate to severe chondromalacia, particularly since the product provides a hard, self-centering meniscal device that is “devoid of physical means that fix its location”. In so doing, the device of Fell et al. tends to require a significant amount of intact cartilage and meniscus. Applicant’s own products to date, including those improved embodiments described herein, have been largely geared toward more elderly patients, where such healthy cartilage is lacking. In turn, Applicant’s devices tend to provide angular correction and improved anchoring of the implant at the joint surface.

In spite of developments to date, there remains a need for a joint prosthesis system that provides an optimal combination of properties such as ease of preparation and use, and performance within the body.

BRIEF DESCRIPTION OF THE DRAWING

In the Drawing:

Figure 1 shows top and side perspectives of a preferred preformed knee implant prepared according to the present invention.

5 Figure 2 shows an embodiment in which preformed components adapted to be inserted and assembled *in situ*.

Figure 3 shows an alternative embodiment in which preformed components are employed.

Figures 4 and 5 show an embodiment in which a substantially open (saucer-shaped) mold is inserted into the joint site, to be filled with a corresponding curable biomaterial *in situ*.

Figure 6 shows a variety of alternative embodiments that include one or more preformed component.

Figure 7 shows a variety of alternative means for anchoring a preformed component such as that shown in Fig. 6d.

Figure 8 shows a further variety for anchoring or stabilizing a preformed portion by the use of ancillary portions and/or surface texture.

Figure 9 shows a variety of embodiments in a substantially closed (balloon like) mold is adapted to be inserted into the joint site and filled with a corresponding curable biomaterial.

20 Figure 10 shows a mold adapted for use as an acetabular mold in connection with the replacement of the articulating surface in a hip.

Figure 11 shows a patella femoral joint form suitable for use in combination with the method and system of this invention.

SUMMARY OF THE INVENTION

The present invention provides a method and system for the creation or modification of the wear surface of orthopedic joints, and particularly articulating joints such as the knee. In one preferred embodiment, the method relies, at least in part, upon the manner in which the various stages of curing a curable biomaterial, and in turn, the various stages of forming a component from the cured or curing biomaterial, can be correlated and optimized in a desired manner. In turn, such a method provides the ability to both generally and specifically form the component for use *in situ*.

The present invention includes a variety of embodiments, each of which preferably includes one or more components that are formed *ex vivo*, and that are adapted to be inserted and finally formed or assembled *in situ* in order to provide a final prosthesis and articulating joint surface. Examples of the various embodiments include, for instance,

- 1) one or more components that are each partially molded *ex vivo*, in a manner that permits the component to be inserted and finally formed *in situ*,
- 2) a plurality of preformed components adapted to be assembled *in situ*, for instance in an overlapping or interlocking fashion,
- 3) an insertable open (e.g., saucer shaped) mold, adapted to be inserted and positioned within the joint site, and there used in combination with a flowable biomaterial adapted to be delivered to the open mold *in situ*, under conditions that permit the flowable biomaterial to cure in contact and/or combination with the mold in order to form a final prosthesis,
- 4) one or more generally extensible envelope (e.g., balloon- type) molds, adapted to be positioned and filled *in situ* with corresponding curable biomaterials, one or more of the molds themselves providing one or more regions of generally non-extensible, preformed material. In

one embodiment, for instance, a plurality of such envelope portions (e.g., a bi-compartmental single envelope) can be adapted for use on both the medial and lateral tibial surfaces, respectively.

By the selection and use of a suitable biomaterial, and other features as described herein, the present invention provides an optimal combination of benefits, as compared to methods previously described. Such benefits include those that arise in the course of preparation and storage (e.g., sterility, storage stability), those that arise in the surgical field itself (e.g., ease of use, adaptability, predictability), and those that arise in the course of long term use within the body (e.g., biocompatibility, moisture cure characteristics, tissue congruity and conformability, retention, wear characteristics, and physical-mechanical properties).

In one preferred embodiment, the method and system involve the preparation and use of partially cured components that can be formed outside the body, for insertion and placement into the body, and that can then be further formed within the joint site in order to enhance conformance. The ability to finally form one or more components *in situ* provides various additional benefits, such as increased control over the overall size and shape of the final prosthesis, improved shape and compliance of the surface apposing natural bone, and finally, improved shape and compliance of the opposite, articulating surface.

As used herein, the word "cure", and inflections thereof, will refer to the extent to which a curable biomaterial, as used to form a component of this invention, has begun or completed whatever physical- chemical reactions may be contemplated in the course of fully forming the component, at the surgical site, for long term use *in situ*. In turn, the biomaterial can be considered as uncured (as in component parts that have not yet been mixed or compositions that have not yet been activated), or it can be partially cured (e.g., wherein the components have been

mixed, or compositions activated, under conditions suitable to begin the curing process), or it can be fully cured (e.g., in which case, whatever chemical reactions may have occurred have substantially subsided). Generally, uncured compositions are sterile, storage stable, and often flowable, though are typically not yet formed or capable of being formed.

5 Curing compositions, by contrast, generally begin as flowable compositions, but become nonflowable over a finite time period as they begin to gel or set. Curing compositions can also be minimally formed, e.g., outside the body by the use of molds and/or suitable shaping tools, and/or within the body, as by the initial positioning of the component on supporting bone and by the repositioning of opposing, articulating bone surfaces. Thereafter, it is contemplated that certain compositions of this invention can be further formed, over time, as by the gradual effect of articulating bone in the course of long term use.

As also used herein, the word “form”, and inflections and variations thereof, will refer to the manner and extent to which a component has been sized and shaped, in either a general and/or specific manner, for use at a joint site. In turn, the forming of such a component can occur either *ex vivo* and/or *in vivo*, as well as in a general manner (e.g., by the use of an *ex vivo* mold or tools) and/or a specific manner (e.g., by final curing in apposition to supporting bone and/or opposing articulating bone surfaces), as well as combinations thereof.

20 A component can be “specifically” formed in this manner in order to conform the component (and particularly its surfaces) to the corresponding specific shapes and dimensions of bone *in situ*, including both supporting bone surfaces and/or opposing (e.g., articulating) bone surfaces. Such specific conformation, in turn, can be used to improve a variety of characteristics of the final implant, including comfort, mechanical performance, and/or long term stability. Such conformation can also include aspects in which one or more components, or the composite

prosthesis, are “conformed” in correspondence with the joint site (e.g., by final shaping and curing processes that occur *in situ*).

Such conformation can also include aspects in which the components, or prosthesis itself, are adapted to be “deformed” within the site, as by the application of force. For instance, a substantially fully formed component can be provided to have sufficient mechanical properties (e.g., strength and resilience) to permit it to be inserted into a joint site and effectively deformed under normal anatomic forces. For instance, a substantially convex component can be deformed to assume the corresponding concave shape *in situ*, in , while retaining sufficient resilient strength to tend towards its original convex shape (e.g., analogous to the manner in which a locking washer can be deformed in use, while tending toward its original shape). Preferably, a final knee component is adapted to be deformed under conditions of use within the body (e.g., under physiologic load), while maintaining desired size and tibial congruency, and in a manner that provides desired fit and thickness for desired angular correction.

Hence a “preformed” component will generally refer to a component that is at least partially formed *ex vivo*, as by the surgeon’s selection and use of an appropriately sized *ex vivo* mold. Such a preformed component can be specifically formed as well, including in an *ex vivo* fashion, as by the use of a customized mold that is itself reflective of the particular dimensions and contours of the intended joint site. Such customized molds can be prepared, for instance, by the use of external imaging means, and/or by the appropriate use of negative and/or positive molds taken at the tissue site. Optionally, and preferably, the preformed component is specifically formed, in whole or in part, by being positioned *in situ*, prior to the completion of the curing process, and in apposition to both supporting bone and opposing bone surfaces. Once positioned within the joint site, any such component or prosthesis can be adapted to be deformed

in order to improve its retention and/or performance *in situ*, e.g., resiliently deformed upon release of distracting forces and repositioning of the opposing bone surface.

For instance, a preformed composition is provided, formed initially by the *ex vivo* onset of cure, in which the composition can be implanted within on the order of 10 seconds to several days of the onset of cure, preferably within about 30 seconds to about 10 minutes, and more preferably within about one to about five minutes, while maintaining a surface exotherm of less than about 50C, and more preferably less than about 45C once positioned within the body.

Once positioned *in vivo*, preferred preformed components of this invention are adapted to be finally shaped, for a period of between about 10 seconds and one or more hours, and more preferably between about one minute and about five minutes. The lower limit is defined largely by the time it takes to effectively reposition bone, or otherwise re-establish suitable force on the implant. The upper limit, in turn, is generally defined by the susceptibility of the implanted composition to further deformation or shaping. Such final shaping is generally accomplished, at least in part, under the force brought about by repositioning articulating bone surfaces. In one preferred embodiment, the partially cured composition is implanted under conditions that permit it to deform less than about 15%, preferably less than about 10%, and most preferably less than about 5%, under physiologic forces, while maintaining tibial congruency and imparting desired angular correction.

Hence, a particularly preferred preformed component of this invention can be implanted within an initial about one to about five minutes of the onset of its formation, and once implanted can be further molded or formed for a further period of about one to about five additional minutes, in a manner that permits the resultant implant to substantially retain a desired final form and function.

In addition to its immediate use in such joints as the knee, the system of the present invention provides particular advantages when applied to ball and socket joints, such as the hip. In one such embodiment, a balloon can be filled with a biomaterial as described herein, and inserted and positioned within the acetabulum, prior to or following filling, to provide a soft, conformable, durable lining for the placement of a hip prosthetic portion.

In a further embodiment, the method and system involve the preparation and use of one or more partially or fully cured component(s) formed outside the body, for insertion and placement into the body and optionally further fitting and securing at the joint site. These preformed component(s) typically require less manipulation at the bedside and allow for alternative methods of terminal sterilization, and final inspection and release at the manufacturing site.

DETAILED DESCRIPTION

The method and system (e.g., preformed component(s) and/or curable biomaterial and mold) can be used to prepare a final prosthesis, *in vivo*, that provides a first major surface in apposition to and retained upon the supporting bone itself, and a second (generally substantially parallel and opposite) major surface adapted to provide a wear surface for opposing (e.g., articulating) bone. By “retained upon” it is meant that the final prosthesis is maintained in a desired position upon the supporting bone surface in a manner suitable for its intended use, e.g., by the use of one or more anchor points, by the use of adhesive or other suitable interface materials, by the use of sutures, staples, and the like, and/or by a mechanical lock achieved by the combination of a bone-contacting surface suitably conformed or conformable to the terrain of

supporting bone, together with the retaining (and optionally including deforming) effect achieved upon repositioning opposing articulating bone surface.

The first and second major surfaces can be provided in any suitable manner, for instance,

1) by the preparation and insertion of a single partially cured and generally preformed component into the joint, preferably under conditions that permit the component to become further, and specifically, formed *in vivo*, 2) by adding a flowable biomaterial to an initial preformed component (e.g., in the shape of a balloon or open mold) positioned at the tissue site, 3) by placing one or more fully cured and preformed components at the tissue site and optionally further fitting, adapting and/or securing the component(s) as needed, and/or 4) by assembling one or more preformed components *in situ* (e.g., side by side in an interlocking fashion upon the surface) such that the assembled components cooperate to provide the first and second major surfaces.

In addition to the partially or fully cured preformed component(s) and/or curable biomaterial and related molds, the method and system of this invention include the optional use of various additional materials and/or steps, e.g., to prepare the bone surface itself, to provide suitable interfaces (e.g., adhesive interfaces and/or protrusions that can be further secured to the joint site or by smoothing of the femoral condyle or tibial plateau as needed), to treat one or more surfaces in order to provide them with different or improved properties as compared to the inherent properties of the material providing the surface, and the like. Examples of such materials include, for instance, the use of adhesive materials, tissue in-growth stimulators, and fibrous materials (e.g., webs adapted to tether the implant and/or to facilitate fibrous tissue ingrowth).

5 The partially or fully cured preformed component(s) can themselves each provide uniform or non-uniform properties, and can be provided in a plurality or range of styles and sizes. These components can be designed to conform to lateral or medial compartments, or both, and to right or left knees, or both. In a preferred embodiment, all embodiments can be inserted into the joint site in a minimally invasive fashion. By “minimally invasive”, in this context, it is meant that the procedure of sizing, inserting, positioning and forming the prosthesis, *in situ*, can preferably be accomplished without the need for open, invasive incisions of the type conventionally used for inserting total knee prostheses. In a preferred embodiment, the partially cured preformed components can be further formed and fully cured *in vivo* to enhance compliance with the joint site.

The surface of the partially or fully cured preformed component(s) can also be modified to provide any desired properties (e.g., promote adhesion), such as by the design and use of polymers themselves or by surface treatment of the fully cured or curing embodiments to provide suitable reactive groups such as amines, hydroxyl groups, or other reactive or hydrogen bonding functionalities. Similarly, the partially cured preformed component or fully cured component, including balloons or composite materials, can be provided with appropriate surface coatings, e.g., biologically active agents to promote desired tissue interactions, including tissue or cellular adhesion, such as those selected from the group consisting of cytokines, hydroxyapatite, collagen, and combinations thereof.

20 In one embodiment of this invention, partially cured, and generally preformed components are inserted into the joint site, and there further and specifically formed to enhance compliance. In an alternative embodiment, fully cured components in the shape of a balloon or open mold are employed to provide a final composite material by inserting the balloon or mold

into the joint and there filling it with a biomaterial that cures *in situ* and conforms with the joint site. In another alternative embodiment, the fully cured component(s) are provided and inserted into the joint either singly or piecemeal and optionally further fitted and secured *in vivo*.

As an example of the first such embodiment, the invention provides an open *ex vivo* mold, adapted to approximate the desired dimensions of the joint site, and to receive a curable biomaterial. A suitable mold can be formed, for instance, from the use of conventional materials such as silicone materials, that permit the curing biomaterial component to be easily and entirely removed at the desired time. Optionally, the mold can itself be provided with a coating or release liner, including those that can be integrated, in whole or in part, with the component thus formed. Once the flowable biomaterial has been delivered and partially cured in this *ex vivo* mold, and any optional molding or fabricating steps have occurred, the biomaterial can be removed from the mold and inserted into the joint site, under conditions suitable to permit it to be further and finally formed *in vivo* to enhance conformance with the joint site. Optionally, additional *ex vivo* forming steps or features can be performed, e.g., by imparting desired curvature and femoral glide paths, prior to inserting and final forming *in vivo*.

Also, in the course of molding the component *ex vivo*, and/or transferring it to the tissue site, various structures and/or materials can be incorporated into and/or onto the component itself, to enhance its placement, retention and/or performance *in situ*. For instance, the mold itself can be provided in a form sufficient to impart various integral structural features, such as tibial “tabs”, adapted to provide or improve the retention of the component at the tissue site. Such tabs, for instance, can be provided in the form of one or more protrusions integral with the mold itself and adapted to be positioned within and/or affixed to the soft tissue and/or bone *in*

vivo. Examples of such tabs are shown, for instance, in Figure 1, where reference number 18 depicts a raised posterior portion.

An insertable component can also be provided with one or more ancillary portions or protrusions formed of materials other than that used to form the bulk of the component itself.

- 5 For instance, sutures or fibrous materials can be incorporated into or onto the bulk material, for use in improving the initial and/or long term retention of the component *in situ*, e.g, by tethering the prosthesis at the joint site and in a desired position. Such other materials can be temporarily positioned into or upon the mold itself, for instance, or otherwise provided, in a manner that permits them to become integrated into the biomaterial as it fills the mold and becomes partially cured *ex vivo*. With the resulting component positioned *in situ*, the protrusions can be used to tether the implant, by securing them to the surrounding soft tissue and/or bone by use of adhesives, sutures, screws, pins, staples or the like or combinations thereof. The materials can provide both an immediate fixation function, and optionally also a desired long term function, by permitting them to be either absorbed by the body over time, and/or to permit or encourage fibrous tissue ingrowth for long term fixation.

The reinforcing material can be provided in any suitable form, e.g., as fibers (e.g., sutures) or as a uniform woven or non-woven fabric, optionally including one or more reinforcing fibers or layers. A suitable non-woven fabric, for instance, is preferably a material such as is commercially available under the trade name Trevira Spunbond from Hoechst

- 20 Celanese Corporation. The non-woven fabric is generally composed of continuous thermoplastic fiber, needle punched together to yield a felt-like fabric. In addition to fabrics like Trevira Spunbond, other materials such as polyester staple mat, glass fiber mat, as well as other organic and inorganic fiber mats and fabrics can be employed.

Reinforcing fibers can be included within the woven or non-woven fabric, or provided as separate layers of a composite. Such fiber layers can preferably include a directional reinforcing fiber layer of organic or inorganic structural reinforcing fibers such as fiberglass, carbon fibers, aramid fibers which is available from DuPont Corporation under the trade name Kevlar, linear polyethylene or polypropylene fibers such as is commercially available from Allied-Signal, Inc. (now Honeywell) under the trade name Spectra, or polyester fibers. The phrase "reinforcing fiber" can include any fiber which, when used in its own right or added to a composite fabric material, retains or enhances desired structural properties. The fibers can be randomly oriented, or preferentially, they can be oriented in one or more directions. While a number of specific types of materials have been given for use as the reinforcing fiber layer, it will be appreciated by those of ordinary skill in the art that other equivalent-type reinforcing fiber layers can be employed in the practice of the invention. A reinforcing fiber layer can be itself used to secure the prosthesis, or can be attached to a woven or non-woven fiber layer having a number of interstices or pores. Preferably, the reinforcing fiber layer and other fiber layers are secured to each other mechanically, as by conventional stitching, needle punching, stapling or buttons. In the case of certain applications, adhesives can also be used.

Similarly, a partially cured preformed component (and/or ancillary portions incorporated therein) can also be provided with suitable means to improve its ability to retain the component *in situ*, e.g., by the use of surface characteristics that provide improved chemical interactions with the joint site. Such interactions can be achieved by the judicious use of bulk material compositions themselves and/or the use of adhesives or other suitable interface materials. The partially cured, preformed, component can also be physically modified to increase its interactions with joint site, as by surface roughening, etching or cross-hatching, which would tend to provide

increased surface area, and in turn, improved mechanical retention. A partially cured, preformed, component can also be retained by external means that are otherwise secured to the surrounding bone and/or soft tissue by use of adhesives, sutures, screws, pins, staples or the like or combinations thereof. On the major surface opposing articulating bone, the partially cured preformed component can be provided with suitable means as well, intended to improve or alter either its compliance and/or interactions with the opposing bone surface.

In one particularly preferred embodiment, the system includes a partially cured preformed component that is first molded outside of the joint site and adapted to be delivered to a tissue site and there positioned in a fixed position. The mold can be of an open or closed configuration (and/or can involve a one- or multi-step molding process), adapted to preform one or both major surfaces, respectively. Once positioned, the partially cured component is adapted to be initially fit and positioned within the joint site, and to thereafter become better conformed to the specific dimensions and/or terrain (e.g., anatomic structure) of the joint site *in vivo*. Optionally, and preferably, the molds are designed to yield components that have optimum adhesion and conformance to the joint sites. The molds may also be heated during the *ex vivo* partial curing process to optimize component properties or to provide a component that is more formable *in vivo*.

In an alternative preferred embodiment, the method and system involve the preparation and use of one or more fully or partially cured component(s) formed outside the body, for insertion and placement into the body and optionally further fitting and securing at the joint site. In one embodiment, the invention provides a single preformed component that is inserted into the joint site and optionally further fitted or secured as needed. In another embodiment, the invention provides a plurality of preformed components, formed of the same or different

materials, and adapted to be delivered and positioned at the tissue site in a manner that provides a final composite. The components can be combined at the site in any suitable fashion, e.g., by providing a mechanical lock and/or by the use of interfacial materials such as adhesive layers. The components can be combined in any suitable fashion, e.g., as layers upon the bone, or as individual side-by-side components adapted to traverse the bone surface when combined. The use of preformed component(s) can require less manipulation at the bedside and allow for alternative methods of terminal sterilization, and final inspection and release at the manufacturing site. The various means of retaining partially cured preformed components, discussed herein, can be adapted to work with fully cured preformed components.

The method and system of this invention can be used for repairing a variety of mammalian joints, including human joints selected from the group consisting of the tibial plateau of the knee, the acetabulum of the hip, the glenoid of the shoulder, the acromion process of the shoulder, the acromio-clavicular joint of the shoulder, the distal tibial surface of the ankle, the radial head of the elbow, the distal radius of the forearm, the proximal phalanx surface of the great toe, the proximal metacarpal surface of the thumb, and the trapezium of the wrist.

Those portions or combinations of preformed component(s) that contact the bone surface are preferably adapted to physically conform closely to the prepared bone surface, e.g., to its macroscopic physical contours. Such conformation can be provided or enhanced in any suitable manner, e.g., 1) by providing a partially cured preformed component that is first made in an *ex vivo* mold and then adapted or modified to conform to the surface (e.g., by further forming *in vivo*), and/or 2) by use of a preformed balloon or composite mold material that is inserted into the joint site and filled with a flowable biomaterial that cures *in vivo* so that it conforms with the joint site and/or 3) by the use of fully cured preformed component(s) that has optimum geometry

for biomaterial compliance once placed in the joint site and/or 4) by the preparation and use of a suitable (e.g., thin) interface material between bone and preformed component (e.g., adhesive, filler, or cement material), and/or 5) by the use of physical restraining means, such as adhesives, pins, staples screws, sutures or the like that are attached to protrusions in the component itself or
5 to an external means of securing it.

The method and system of this invention will be further described with reference to the Drawing, wherein

Figure 1 shows a top and side perspective of a preferred preformed knee implant (10) prepared using an *ex vivo* mold according to the present invention. The implant provides a first major surface (12) adapted to be positioned upon the tibial surface, and a generally planar second major surface (14) adapted to be positioned against the femoral condyle. In a typical embodiment, the second major surface, in turn, is preferably provided with a femoral glide path (16) to facilitate its performance *in situ*, in the form of a generally central oval depression about 1 mm to about 5mm deep at its lowest point (2 mm as shown) and about 30 mm to about 50 mm in length by 10 mm to 30 mm in width (40 mm by 20 mm as shown). Those skilled in the art, given the present description, will readily determine the actual dimensions for optimal use, in both absolute and relative terms, depending on such factors as the actual joint size and desired results (e.g., angular correction). As shown, the implant is also provided with a raised tibial projection (18), adapted to catch the posterior portion of the tibial plateau. The implant can have
20 dimensions on the order of between about 40 to about 60 mm in the anterior-posterior dimension, between about 30 mm to about 40 mm in the medial-lateral dimension, and a maximum thickness (at the posterior lip of between about 10 mm and about 20 mm.

Figure 2 shows an embodiment in which a plurality of preformed components are adapted to be inserted and assembled *in situ* to provide the final implant (20). Figure 2a shows an embodiment, in which preformed components (22 through 25, respectively) are assembled in a side-by-side manner sequentially, and *in situ*, and upon the tibial surface. The matable preformed sections each provide at least a portion of the resultant bone-contacting surface and wear surface, as well as one or more portions adapted to provide a mechanical lock with one or more respective other portions. The mechanical lock can be achieved in any suitable manner, as by the provision of corresponding male and female portions, respectively. The portions can be mated, *in situ*, e.g., in a press fit or sliding manner, in order to attach the respective components. As can be seen in the raised perspective of the same embodiment, and Figure 2b, in the resultant assembly, the combined components cooperate to provide both a tibial bone-contacting surface (28) and a wear surface (26).

In the alternative embodiment of Figure 3, rather than being positioned in a side-by-side fashion across the bone surface (as in Figure 2), a final implant is provided using interlocking preformed components (shown in this case as portions 31 through 33, respectively) are instead provided in a form that permits them to be stacked upon each other, e.g., by layering or sliding them onto each other, and positioned upon the surface, *in situ*. The portions can be assembled in any suitable fashion, e.g., entirely on the tissue site, entirely *ex vivo*, or in varying combinations as desired. Optionally, and preferably, the generally planar portions are provided with corresponding matable portions, e.g., in the form of grooves and tabs to provide a sliding fit, or a depression and corresponding projection to provide either a press fit, snap fit, or other suitable fit sufficient to prevent lateral displacement to the extent desired. The resultant formed prosthetic implant can be provided with various features as described herein, including desired molded

portions adapted to provide better fit or performance. Top portion (31) is particularly well suited to provide a desirable wear surface, while one or more intermediate portions (as shown by element 32) are adapted to provide an optimal combination of such properties as thickness, cushioning, and angular correction. As shown the lowermost portion (33) is shown with a projection (34) adapted to be retained within a corresponding anchor hole or suitable depression formed into the bone itself. Figures 3b and 3c provide generally bottom and top views, respectively, showing the manner in which the portions can be combined in a layered fashion.

In the embodiment of Figure 3, preformed layers are shown having protrusions adapted to be positioned in a corresponding indentation within each underlying layer (or bone), in order to form a compact stack. In such an embodiment, the corresponding system will typically include at least two preformed components, including the initial, bone-contacting component, and final component providing the wear surface. The system can provide one or more intermediate layers, e.g., the number and/or selection of which can be used to provide a final desired height to the overall composite, and/or to provide differing properties (e.g., with respect to compressibility, resilience, tissue ingrowth), and/or to provide improved retention between the first and final components.

Figure 4a shows an embodiment in which a substantially open (saucer-shaped) mold (40) is inserted into the joint site, to be filled with a corresponding curable biomaterial *in situ*. The top (42) of the mold is open to receive biomaterial (not show), while the bottom (44) provides a lower major surface (46) adapted to contact bone and terminates in a filled protrusion (48) adapted to be positioned within a corresponding anchor point drilled in the bone itself. The anterior edge (50) of the cup is substantially perpendicular to the plane of the cup itself, while the

posterior edge (52) is tapered (and optionally raised) to accommodate the corresponding shape of the tibial spine.

As shown, and for use in an adult human, the *ex vivo* mold accommodates a predetermined volume of biomaterial of on the order of about 5 ml to about 15 ml. As a further advantage of this invention, the amount of biomaterial actually can be predetermined and controlled to correspond with the *ex vivo* mold volume. In addition the *ex vivo* molds are designed for optimum sizing and conformance to the joint site and MRI software may be used to chose best mold for joint site. Implant thickness and hence angular correction can be controlled in this way.

Figure 4b shows a bottom perspective view of the mold apparatus of Figure 4a, showing the filled protrusion (48). The posterior edge portion (and particularly the posterior mesial edge portion, as seen in the figure) can be seen as provided with a groove or indentation (54), again to accommodate the typical shape of the corresponding tibial spine. Overall, the mold can be seen as assuming a generally kidney-shaped configuration, adapted to correspond with the tibial surface. Such a mold can be provided in a plurality of sizes, and shapes, to be selected at the time of use to accommodate the particular patient's needs and surgeon's desires.

Figures 5a and 5b show the mold of Figure 4a being positioned upon a tibial surface (Fig. 5a), with the protrusion positioned within a corresponding anchor point, and (in Fig. 5b) with the tip of a biomaterial delivery cannula (56) positioned upon it, and with flowable biomaterial (58) being shown in the course of delivery.

Figure 6 shows a variety of alternative embodiments that include one or more preformed component. Fig. 6a shows a simple wedge shaped embodiment (60), in which the posterior portion (62) is significantly increased in size as compared to the anterior (64). Fig. 6b shows an

implant (66) molded to provide portions (here, layers) having differing wear characteristics, including a preformed top having improved wear as compared to the separately formed bottom portion (70). Fig. 6c, by comparison, shows a plurality of components (72) adapted to be positioned and assembled in situ at the time of surgery. These include an upper portion (74) having improved wear characteristics as compared to the others, a bottom portion (78) being suitably formed to the patient's geometry and desired angular correction, and one (or more) central portions (76) adapted to be positioned between the top and bottom portions to achieve desired properties such as overall thickness, angles, and/or physical chemical properties (such as moduli).

The embodiment of Figure 6d shows a single piece (80) as might be cut from preformed material at the time of surgery, while Figure 7 shows a variety of alternative means for anchoring a preformed component such as that shown in Fig. 6d. These include the use of a grout (82) or other suitable interface material as shown in Fig. 7a; the use of a separate external retaining device (84) as shown in Fig. 7b; the use of externally provided pins, screws, sutures, etc. as exemplified by elements (86) which generally traverse the body itself as in Fig. 7c; and the use of one or more anchor portions (88) positioned along one or more suitable surfaces as shown in Fig. 7d.

Figure 8 shows a further variety for anchoring or stabilizing a preformed portion by the use of ancillary portions and/or surface texture, including a roughened surface (90) as in Fig. 8a; or tabs (e.g., provided by fabric or suture like materials) as shown as elements 92 and 94 of Figs. 8b and 8c, respectively. In practice, the preformed components can benefit from any suitable combination of the various features and embodiments described or shown herein.

Figure 9 shows a variety of embodiments in a substantially closed (balloon like) mold is adapted to be inserted into the joint site and filled with a corresponding curable biomaterial, the mold itself providing a preformed articulating wear surface, including Fig. 9a which shows an inflatable balloon portion (96) that includes an integral preformed wear surface and portion (98), as well as a lumen (100) adapted to fill the inflatable portion with flowable biomaterial. Fig. 9b shows a corresponding balloon (102) though without a preformed portion, and including its biomaterial lumen (104). Although not shown, the balloon of this or any embodiment can include various interior and/or exterior surface coatings, and can have regions and/or layers having different desired physical-chemical properties (such as porosity). Fig. 9c shows a bi-compartmental closed balloon-like mold (106), wherein each compartment is adapted to conform to a respective medial or lateral tibial surface.

Figure 10 shows a mold adapted for use as an acetabular mold (110) in connection with the replacement of the articulating surface in a hip, when filled with biomaterial, the mold forming a concave portion adapted to retain a corresponding femoral head. The mold is shown providing a thin generally cup-shaped mold adapted to be filled in any suitable form (e.g., using a removable conduit (not shown) attached to the space between inner and outer sealed layers (116 and 114, respectively) forming the mold.

Figure 11 shows a patella-femoral joint form suitable for use in combination with the method and system of this invention. As shown in the views of 11a through 11c, the form includes a silicone or other suitable pad material (122) having aluminum or other suitable stay portions (124) and terminal handle or grasping portions (126). In use, with the knee at a generally 45 degree angle, the piece is formed to the femoral bone surface, with its form maintained by bending the aluminum stays. With anchor points cut into the femoral bone, if

desired, the form is held tight against the bone with the upper handle held away from bone to permit the delivery of curable biopolymer between the form and the bone. As polymer is placed onto the bone (and into any anchor points) the form is maintained for a time sufficient to suitably form the polymer, whereafter it can be removed.

5 As described in Applicant's co-pending US provisional application 60/228,444, the present application describes a method and system for the creation or modification of the wear surface using an implanted material fixed to the support structure of the original wear surface, to generally conform to the shape of the original surface in a mammal. A method or system where the end of the bony surface is a rotating, sliding or rolling surface, such as in the knee, finger, hip, toe, spine, wrist, elbow, shoulder, ankle, or TMJ joint. The implant will function:

- a) as a spacer,
- b) as an impact absorber
- c) as a surface with improved coefficient of friction (as compared to the diseased surface), and/or
- d) to increase the weight bearing area and improve congruency of the joint surface (as compared to the diseased condition).

The method and system of this invention can be applied to areas of aseptic necrosis, such as the nevecular bone in the wrist. The material to be implanted consists of a plurality of materials, such as polymers, including polyurethane, polyethylenes, polyureas, polyacrylates, polyurethane acrylates, hydrogels, epoxies and/or hybrids of any of the above.

20

In an alternative embodiment, the surface can be provided by any of a series of metals, including titanium, stainless steel, cobalt chrome millithium alloys and tantalum. Other surface materials can include various ceramics and biologic polymers.

The implantable material for the resurfacing can be formed ex vivo and/or in vivo as an injectable material that sets up to the molded shape. The methods for changing state from liquid to solid state include cooling or heating, the passage of time, which allows for a change of state, or a chemical reaction between different reactants. The reaction can be exothermic or
5 endothermic. The set-up can be light activated or chemically catalyzed or it could be heat activated. Examples of such systems include flowable polymers of two or more components, light activated polymers, and polymers cured either by catalysts or by heat, including body heat. Molds can be used in the form of balloons, dams or retainers. They can be used in combination with the local anatomy to produce the desired shape and geometry. Molds can be of materials that are retained and becomes part of the implant or could be removed after curing of the biomaterial component.

In an alternative embodiment, the material would be semi-solid and could be shaped and then set up in vivo. This would allow for the minimally invasive application, either through an arthroscopic portal or through a small mini arthrotomy. As a further embodiment, the material could be synthesized ex vivo and then machined to fit using imaging to pre-determine the desired geometry and size of the implant. As a further alternative, a range of implant sizes could be provided and sizing could be accomplished during the procedure. An ex vivo mold could be fit using molding materials and the implant could be molded on site just prior to implantation.

Fixation methods for the implant would include biologic glues to glue the implant to the
20 underlying surface, trapping of the implant into a cavity on the surface that causes a mechanical lock, using various anchors to the underlying structure and fixing the implant to that surface or using mold retainers and/or screws, staples, sutures or pins. In alternative embodiment, anchors

in the underlying structure may be used for fixing the implant to that surface and we may also use a tissue ingrowth system to secure anchoring.

In the preferred embodiment, the patient will have a diagnosis of osteoarthritis and have loss of cartilage on the articulating surface. A determination will be made of the amount of correction needed for the reestablishment of a normal angle of articulation. The ligaments will be balanced so that there is no loss of range of motion with the implant in place and the surface will be placed in such a position that the eventual resulting surface geometry reestablishes the same plane and orientation of the original articular surface.

Access to the site is obtained in a minimally invasive way. In a preferred embodiment, this is accomplished through arthroscopic means with arthroscopic portals. In an alternative embodiment, the access is accomplished by a mini arthrotomy with a small incision that allows access to the joint without sacrificing nerves, vessels, muscles or ligaments surrounding the joint. In the preferred embodiment fibrillated articulating cartilage that is degenerated is removed down to the subchondral surface. The surface is dried and prepared for appropriate anchoring. This may include anchor points that give a mechanical lock or that alternatively simply supply horizontal and lateral stability. The surface may be prepared by drying and roughening in case a tissue adhesive is used. Pre-made anchors may be installed. These may be made of various metallic materials or of polymers and may consist of pegs that would extend up through the implant to anchor it to the underlying surface. This surrounding subchondral bone may be roughened to enhance tissue ingrowth or implant adhesion. The final geometry of the implant may be determined by a dam or mold that is placed on the joint at the time the material is implanted, when the implant is installed using an *in situ* cured technique (in the manner shown in Figures 1 and 4 of Applicant's provisional parent application).

For pre-made material formed at the surgical site within a mold, various forms of stabilization could be used, including anchor points or titanium screws. Alternatively, the pre-made material could be made off site to the specs developed from imaging of the patient's joint surface. In a third embodiment, multiple sizes could be made off site and the selection of the appropriate implant size could be chosen at the time of surgery. Two alternatives shown in Figure 2 of the parent provisional application include a single segment that can be installed through a portal or a series of segments that can be installed through a portal and locked together once inside the joint. They would be placed sequentially and then anchored to the bone by anchor points cut in the bone or by screws or tissue ingrowth. Finally, a robot, a jig or other cutting fixture could be used to prepare the bony surface for the pre-made implant to a fixed geometry of the anchor point.

Both the preformed component(s) and flowable biomaterial, if used, can be prepared from any suitable material. Typically, the materials include polymeric materials, having an optimal combination of such properties as biocompatibility, physical strength and durability, and compatibility with other components (and/or biomaterials) used in the assembly of a final composite. Examples of suitable materials for use in preparing the preformed component(s) may be the same or different from the *in situ* curing biomaterial, and include polyurethanes, polyethylenes, polypropylenes, Dacrons, polyureas, hydrogels, metals, ceramics, epoxies, polysiloxanes, polyacrylates, as well as biopolymers, such as collagen or collagen-based materials or the like and combinations thereof.

Examples of suitable materials for use in preparing the flowable biomaterial, if used, include polyurethanes, polyureas, hydrogels, epoxies, polysiloxanes, polyacrylates, and combinations thereof.

In a presently preferred embodiment, the preformed component(s) and the flowable biomaterial, if included, each comprise a biocompatible polyurethane. The same or different polyurethane formulations can be used to form both the preformed component(s), e.g., by an injection molding technique, as well as for the flowable biomaterial, if present.

5 Suitable polyurethanes for use as either the preformed component or biomaterial can be prepared by combining: (1) a quasi-prepolymer component comprising the reaction product of one or more polyols, and one or more diisocyanates, and optionally, one or more hydrophobic additives, and (2) a curative component comprising one or more polyols, one or more chain extenders, one or more catalysts, and optionally, other ingredients such as an antioxidant, and hydrophobic additive.

In the embodiment in which an *in situ* curing polymer is used, the present invention preferably provides a biomaterial in the form of a curable polyurethane composition comprising a plurality of parts capable of being mixed at the time of use in order to provide a flowable composition and initiate cure, the parts including: (1) a quasi-prepolymer component comprising the reaction product of one or more polyols, and one or more diisocyanates, optionally, one or more hydrophobic additives, and (2) a curative component comprising one or more polyols, one or more chain extenders, one or more catalysts, and optionally, other ingredients such as an antioxidant, hydrophobic additive and dye. Upon mixing, the composition is sufficiently flowable to permit it to be delivered to the body, and there be fully cured under physiological
20 conditions. Preferably, the component parts are themselves flowable, or can be rendered flowable, in order to facilitate their mixing and use.

The flowable biomaterial used in this invention preferably includes polyurethane prepolymer components that react either *ex vivo* or *in situ* to form solid polyurethane ("PU").

2057E0.T0936003
The formed PU, in turn, includes both hard and soft segments. The hard segments are typically comprised of stiffer oligourethane units formed from diisocyanate and chain extender, while the soft segments are typically comprised of one or more flexible polyol units. These two types of segments will generally phase separate to form hard and soft segment domains, since they tend to be incompatible with one another. Those skilled in the relevant art, given the present teaching, will appreciate the manner in which the relative amounts of the hard and soft segments in the formed polyurethane, as well as the degree of phase segregation, can have a significant impact on the final physical and mechanical properties of the polymer. Those skilled in the art will, in turn, appreciate the manner in which such polymer compositions can be manipulated to produce cured and curing polymers with desired combination of properties within the scope of this invention.

The hard segments of the polymer can be formed by a reaction between the diisocyanate or multifunctional isocyanate and chain extender. Some examples of suitable isocyanates for preparation of the hard segment of this invention include aromatic diisocyanates and their polymeric form or mixtures of isomers or combinations thereof, such as toluene diisocyanates, naphthalene diisocyanates, phenylene diisocyanates, xylylene diisocyanates, and diphenylmethane diisocyanates, and other aromatic polyisocyanates known in the art. Other examples of suitable polyisocyanates for preparation of the hard segment of this invention include aliphatic and cycloaliphatic isocyanates and their polymers or mixtures or combinations thereof, such as cyclohexane diisocyanates, cyclohexyl-bis methylene diisocyanates, isophorone diisocyanates and hexamethylene diisocyanates and other aliphatic polyisocyanates. Combinations of aromatic and aliphatic or arylalkyl diisocyanates can also be used.

The isocyanate component can be provided in any suitable form, examples of which include 2,4'-diphenylmethane diisocyanate, 4,4'-diphenylmethane diisocyanate, and mixtures or combinations of these isomers, optionally together with small quantities of 2,2'-diphenylmethane diisocyanate (typical of commercially available diphenylmethane diisocyanates). Other
5 examples include aromatic polyisocyanates and their mixtures or combinations, such as are derived from phosgenation of the condensation product of aniline and formaldehyde. It is suitable to use an isocyanate that has low volatility, such as diphenylmethane diisocyanate, rather than more volatile materials such as toluene diisocyanate. An example of a particularly suitable isocyanate component is the 4,4'-diphenylmethane diisocyanate ("MDI"). Alternatively, it can be provided in liquid form as a combination of 2,2'-, 2,4'- and 4,4'- isomers of MDI. In a preferred embodiment, the isocyanate is MDI and even more preferably 4,4'-diphenylmethane diisocyanate.

Some examples of chain extenders for preparation of the hard segment of this invention include, but are not limited, to short chain diols or triols and their mixtures or combinations thereof, such as 1,4-butane diol, 2-methyl-1,3-propane diol, 1,3-propane-diol ethylene glycol, diethylene glycol, glycerol, cyclohexane dimethanol, triethanol amine, and methyldiethanol amine. Other examples of chain extenders for preparation of the hard segment of this invention include, but are not limited to, short chain diamines and their mixtures or combinations thereof, such as dianiline, toluene diamine, cyclohexyl diamine, and other short chain diamines known in
20 the art.

The soft segment consists of urethane terminated polyol moieties, which are formed by a reaction between the polyisocyanate or diisocyanate or polymeric diisocyanate and polyol. Examples of suitable diisocyanates are denoted above. Some examples of polyols for

preparation of the soft segment of this invention include but are not limited to polyalkylene oxide ethers derived from the condensation of alkylene oxides (e.g. ethylene oxide, propylene oxide, and blends thereof), as well as tetrahydrofuran based polytetramethylene ether glycols, polycaprolactone diols, polycarbonate diols and polyester diols and combinations thereof. In a preferred embodiment, the polyols are polytetrahydrofuran polyols ("PTHF"), also known as polytetramethylene oxide ("PTMO") or polytetramethylene ether glycols ("PTMEG"). Even more preferably, the use of two or more of PTMO diols with different molecular weights selected from the commercially available group consisting of 250, 650, 1000, 1400, 1800, 2000 and 2900.

Two or more PTMO diols of different molecular weight can be used as a blend or separately, and in an independent fashion as between the different parts of the two part system. The solidification temperature(s) of PTMO diols is generally proportional to their molecular weights. The compatibility of the PTMO diols with such chain extenders as 1,4-butanediol is generally in the reverse proportion to molecular weight of the diol(s). Therefore the incorporation of the low molecular weight PTMO diols in the "curative" (part B) component, and higher molecular weight PTMO diols in the prepolymer (part A) component, can provide a two-part system that can be used at relatively low temperature. In turn, good compatibility of the low molecular weight PTMO diols with such chain extenders as 1,4-butanediol permits the preparation of two part systems with higher (prepolymer to curative) volume ratio. Amine terminated polyethers and/or polycarbonate-based diols can also be used for building of the soft segment.

The PU can be chemically crosslinked, e.g., by the addition of multifunctional or branched OH-terminated crosslinking agents or chain extenders, or multifunctional isocyanates.

Some examples of suitable crosslinking agents include, but are not limited to, trimethylol propane ("TMP"), glycerol, hydroxyl terminated polybutadienes, hydroxyl terminated polybutadienes (HOPB), trimer alcohols, Castor oil polyethyleneoxide (PEO), polypropyleneoxide (PPO) and PEO-PPO triols. In a preferred embodiment, HOPB is used as the crosslinking agent.

This chemical crosslinking augments the physical or "virtual" crosslinking of the polymer by hard segment domains that are in the glassy state at the temperature of the application. The optimal level of chemical cross-linking improves the compression set of the material, reduces the amount of the extractable components, and improves the biodegradability of the PU. This can be particularly useful in relatively soft polyurethanes, such as those suitable for the repair of damaged cartilage. Reinforcement by virtual cross-links alone may not generate sufficient strength for *in vivo* performance in certain applications. Additional cross-linking from the soft segment, potentially generated by the use of higher functional polyols can be used to provide stiffer and less elastomeric materials. In this manner a balancing of hard and soft segments, and their relative contributions to overall properties can be achieved.

Additionally, a polymer system of the present invention preferably contains at least one or more, biocompatible catalysts that can assist in controlling the curing process, including the following periods: (1) the induction period, and (2) the curing period of the biomaterial. Together these two periods, including their absolute and relative lengths, and the rate of acceleration or cure within each period, determines the cure kinetics or profile for the composition. Some examples of suitable catalysts for preparation of the formed PU of this invention include, but are not limited to, tin and tertiary amine compounds or combinations thereof such as dibutyl tin dilaurate, and tin or mixed tin catalysts including those available under the tradenames "Cotin

222", "Formrez UL-22" (Witco), "dabco" (a triethylene diamine from Sigma-Aldrich), stannous octanoate, trimethyl amine, and triethyl amine. In a preferred embodiment, the catalyst is Formrez UL-22 (Witco). In an alternative preferred embodiment, the catalyst is a combination Cotin 222 (CasChem) and dabco (Sigma-Aldrich).

5 The *in vivo* and *ex vivo* cured polyurethanes of this invention can be formed by the reaction of two parts. Part I of which (alternatively referred to as Part A) includes a di- or multifunctional isocyanate or quasi-prepolymer which is the reaction product of one or more OH-terminated components, and one or more isocyanates. Part II of the polyurethane (alternatively referred to as Part B herein) is a curative component that includes of one or more chain extenders and one or more polyols, and one or more catalysts, and other additives such as antioxidants and dyes. For a suitable formed PU, the stoichiometry between Parts I (quasi-prepolymer) and II (curative component), expressed in terms of NCO:OH molar ratio of the isocyanate terminated pre-polymer (Part I) and the curative component (Part II) is preferably within the range of about 0.8 to 1.0 to 1.2 to 1.0, and more preferably from about 0.9 to 1 to about 1.1 to 1.0.

Optionally, a reactive polymer additive can be included and is selected from the group consisting of hydroxyl- or amine-terminated compounds selected from the group consisting of polybutadiene, polyisoprene, polyisobutylene, silicones, polyethylene-propylenediene, copolymers of butadiene with acrylonitrile, copolymers of butadiene with styrene, copolymers of
20 isoprene with acrylonitrile, copolymers of isoprene with styrene, and mixtures of the above.

Suitable compositions for use in the present invention are those polymeric materials that provide an optimal combination of properties relating to their manufacture, application, and *in vivo* use. In the uncured state, such properties include component miscibility or compatibility,

processability, and the ability to be adequately sterilized or aseptically processed and stored. In the course of applying such compositions, suitable materials exhibit an optimal combination of such properties as flowability, moldability, and *in vivo* curability. In the cured state, suitable compositions exhibit an optimal combination of such properties as strength (e.g., tensile and compressive), modulus, biocompatibility and biostability.

When cured, the compositions demonstrate an optimal combination of properties, particularly in terms of their conformational stability and retention of physical shape, dissolution stability, biocompatibility, and physical performance, as well mechanical properties such as load-bearing strength, tensile strength, shear strength, shear fatigue resistance, impact absorption, wear resistance, and surface abrasion resistance. Such performance can be evaluated using procedures commonly accepted for the evaluation of natural tissue and joints, as well as the evaluation of materials and polymers in general. In particular, a preferred composition, in its cured form, exhibits mechanical properties that approximate or exceed those of the natural tissue it is intended to provide or replace.

To achieve these desirable uncured and delivery properties, a “polymer system”, as used herein refers to the component or components used to prepare a polymeric composition of the present invention. In a preferred embodiment, a polymer system comprises the components necessary to form two parts: Part I being an NCO terminated pre-polymer (optionally referred to as an “isocyanate quasi-polymer”). The quasi-polymer of Part I typically includes a polyol component, optionally in combination with a hydrophobic additive component, and an excess of an isocyanate component. Part II of the two component system can include one long-chain polyols, chain extenders and/or cross-linkers, together with other ingredients (e.g., catalysts, stabilizers, plasticizers, antioxidants, dyes and the like). Such adjuvants or ingredients can be

added to or combined with any other component thereof either prior to or at the time of mixing, delivery, and/or curing.

In a particularly preferred embodiment, a polymer system of this invention is provided as a plurality of component parts and employs one or more catalysts. The component parts, including catalyst, can be mixed to initiate cure, and then delivered, set and fully cured under conditions (e.g., time and exotherm) sufficient for its desired purpose. Upon the completion of cure, the resultant composition provides an optimal combination of properties for use in repairing or replacing injured or damaged tissue. In a particularly preferred embodiment, the formulation provides an optimal combination of such properties as compatibility and stability of the biomaterial parts, ex vivo or *in situ* cure capability and characteristics (e.g., extractable levels, biocompatibility, thermal/ mechanical properties), mechanical properties (e.g., tensile, tear and fatigue properties), and biostability.

The volume ratio of the parts can also be used to improve and affect the uncured and curing properties. Compositions having two or more parts, are preferred. Where two parts are used, the relative volumes can range, for instance, from 1:10 to 10:1 (quasi-prepolymer to curative components, based on volume). A presently preferred range is between 2:1 and 1:2. As those skilled in the art will appreciate, given the present description, the optimal volume ratio is largely determined by the compatibility and the stability of part A and B.

In choosing an optimal volume ratio for a given formulation, those skilled in the art, given the present description, will appreciate the manner in which the following considerations can be addressed. The viscosity of the reactive parts, at the temperature used for either injection-molding preformed components, or for *in situ* cure, should provide an acceptable degree of

mixing and flow rate, without causing mechanical failure of any component of the delivery system including cartridge, static mixer, gun and other components.

Preferably, the biomaterial is sufficiently flowable to permit it to be delivered (e.g., injected) into the mold or tissue site. The composition of both reactive parts must be such that these parts are homogeneous and phase stable in the temperature range of the application. Generally, the maximum temperature of the reaction exotherm is proportional to the concentration of the reactive groups in the mixed polymer. A high concentration of the reactive groups might evolve too high reaction exothermal energy and therefore cause thermal damage to the surrounding tissues. The reactive parts will preferably remain substantially liquid in form during mixing.

A desired and stable volume ratio of the components can be achieved in any suitable manner, e.g., by the use of dual-compartment cartridges with constant volume ratio or by using the injectors with delivery rates independently variable for each component.

Compatibility of the composition can also be affected (and improved) in other ways as well, e.g., by pre-heating the components prior to polymer application. To enhance the homogeneity of the components, the components of a preferred composition of this invention are preferably preheated before mixing and delivery, e.g., by heating to about 60 C to about 80 C for about 2 to about 6 hours prior to use. Preferably, the composition parts are cooled back to about 35 C to 37 C before use in injection.

Fully cured polymeric (e.g., polyurethane) biomaterials suitable for use in forming components of this invention provide an optimal combination of such properties as creep and abrasion resistance. Preferably, for instance, the biomaterial provides DIN abrasion values of less than about 100 mm³, more preferably less than about 80 mm³ and most preferably less than

about 60 mm³, as determined by ASTM Test Method D5963-96 (“Standard Test Method for Rubber Property Abrasion Resistance Rotary Drum Abrader”).

2025.04.01.15.00